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**TITLE:**

Hormonal Regulation of Fluid and Electrolyte Metabolism  
during Periods of Headward Fluid Shifts

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**INTRODUCTION:**

In the broadest sense, this project evaluates how spaceflight induced shifts of blood and interstitial fluids into the thorax affect regulation by the central nervous system (CNS) of fluid-electrolyte hormone secretion. Specifically, it focuses on the role of hormones related to salt/water balance, and their potential function in the control of intracranial pressure and cerebrospinal fluid (CSF) composition. Fluid-electrolyte status during spaceflight gradually equilibrates, with a reduction in all body fluid compartments. Related to this is the cardiovascular deconditioning of spaceflight which is manifested upon return to earth as orthostatic intolerance.

**PROJECTS WITHIN THIS WORK UNIT**

**GROUND-BASED STUDIES**

Small Animal Studies

The objective of this task was to determine the role of intracranial pressure (ICP) on the CNS regulation of fluids and electrolytes. To do this it was necessary to measure ICP in conscious unrestrained rats. With some difficulty this was accomplished. Our initial studies showed that an intraventricular (IVT) infusion of angiotensin II increased ICP, and this increase could be blocked with prior IVT administration of vasopressin. Since both of these hormones are endogenous to CSF it is possible that they are involved in ICP regulation either by affecting CSF formation and/or drainage. Recent results indicate that the ICP increase following angiotensin II administration is due to a stimulation of CSF secretion.

As these ICP studies continued we found that prolonged, low volume infusions (0.5  $\mu$ l/min) of artificial CSF into a lateral cerebroventricle more than doubled ICP. If this same volume was infused bilaterally into each lateral cerebroventricle, the rise in pressure was even more pronounced. One explanation for the rise in ICP may be a dilution of the neurochemical control system(s) with artificial CSF that disrupts the pressure autoregulation since artificial CSF does not contain any hormonal or neurochemical factors.

### Primate Studies

When nonhuman primates are water immersed to the neck they show patterns of diuresis and natriuresis similar to humans. Anesthetised animals showed an increase in 1) left ventricular end-diastolic pressure urine flow, sodium/potassium clearance and atrial natriuretic peptide. Experiments by Gilmore, et al. showed that water immersion diuresis in monkeys could not be abolished by removal of neural afferent input to the CNS or with administration of large doses of vasopressin. Perhaps changes in ICP provide an important redundant signal that can trigger renal and hormonal responses to the "hypervolemia" associated with headward fluid shifts in the absence of peripheral pressure/volume sensors. Intracranial pressure measurements have not been made in animals or humans exposed to water immersion or head-down tilt.

To determine the ICP effects of headward fluid displacement we exposed anesthetised rhesus to a short period of -60° head-down tilt followed by a 30 min period of water immersion. The increase in ICP was greater with water immersion. ICP remained elevated throughout the 30 minutes of immersion. A sustained increase in ICP has been observed for immersion periods up to 60 minutes.

Headward fluid shifts and increased atrial pressure are known to stimulate release of ANP and a fall in plasma vasopressin (see above). The role of afferent neural input from the heart has been determined by use of the surgical denervation. Another procedure for acute and reversible cardiac "denervation" is being used to determine the relationship between cardiac afferent input and plasma fluid/electrolyte hormone levels in response to changes in left and right atrial pressure in conscious animals. These studies are in progress.

## **FLIGHT STUDIES**

### Objective

Although fluid-electrolyte balance in rats has not been determined during flight, post-flight hormone measurements and salt-water loading experiments indicate that rats respond to

microgravity by readjustment of their fluid-electrolyte metabolism. The purpose of this investigation was to make post-flight determinations of pituitary oxytocin (OT) and vasopressin (VP) content as possible indicators of changes in hormonal regulation of fluid-electrolyte balance during flight.

Two Cosmos experiments (U.S./U.S.S.R.) have been completed over the past three years. Cosmos 1887 which flew in the Fall of 1987 for 12.5 days and Cosmos 2044 which was a 14 day flight in 1989. In Cosmos 1887, pituitary levels of oxytocin (OT) and vasopressin (VP) were measured in the flight rats and their ground based controls. A significant reduction in both posterior lobe hormones were found in the flight animals when compared to either set of ground-based controls. Difficulties were encountered in landing which cast some doubt on whether the results reflected the effects of spaceflight or simply the conditions associated with the delayed recovery. We had another opportunity to repeat the pituitary measurements as well as determine natriuretic peptide content of atria in Cosmos 2044. The results of this 14 day flight were similar to those from Cosmos 1887. Pituitary OT and VP levels in the flight animals were lower than all the controls including a third control group of tail suspended animals for a direct comparison of results from this model with those from flight. Atrial natriuretic peptide (ANP) content was also reduced in the atria of flight rats.

The reason(s) for the reductions in the tissue contents of these fluid-electrolyte hormones of flight animals are unclear. A simultaneous reduction in pituitary OT and VP occurs with water deprivation that is also accompanied by a loss of body weight. Body weight was not significantly decreased in the flight rats, and postflight measurements of water and food consumption indicated that an appropriate amounts had been consumed. It has yet to be determined if this reduction reflects increased secretion or decreased hormone synthesis and storage. The lack of significant changes in the tail suspended group make this model questionable for use in at least some aspects fluid-electrolyte hormone studies.

#### FUTURE PLANS:

Determine if head-down rats exhibit changes in pituitary and cardiac hormones similar to those observed in animals exposed to 14 days of spaceflight. Study the effects of continuous intraventricular infusions of neuropeptides (8 to 24 hr) on CSF pressure and possible changes in CSF outflow from ependymal and arachnoid surfaces.

## **PUBLICATIONS:**

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**Morrow, B.A, Starcevic, V.P., Keil, L.C., and W.B. Severs. Intracranial hypertension after cerebroventricular infusions in conscious rats. Am. Physiological Society, R1170-R1176 (1990).**

**Starcevic, V.P., Morrow, B.A., Farner, L.A., Keil, L.C. and W.B. Severs. Long-term recording of cerebrospinal fluid pressure in freely behaving rats. Brain Research, 112-117 (1988).**

**Matsukaea, S., Keil, L.C. and I.A. Reid. Role of renal nerves in regulation of vasopressin secretion and blood pressure in conscious rabbits. Am. J. Physiol, F821-F830 (1990).**